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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): Hiatt et al.
Appl. No.: 10/062,467   Confirmation No.: 4901
Filed: February 5, 2002
Patent No.: 7,022,309
Issued: April 4, 2006
Art Unit: 1651
Examiner: David M. Naff
Title: TARGETING MOLECULE LINKED TO AN IMAGING AGENT

Docket No.: 040989/283649
Customer No.: 00826

Decisions & Certificate of Correction Branch
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Certificate
OCT 24 2006
of Correction

REQUEST FOR RECONSIDERATION

Applicants respectfully request reconsideration of the request for the issuance of a Certificate of Correction which was previously submitted on July 31, 2006 for the above-referenced patent. Granting of the correction to Table III, Column 31-32, Lines 6 and 8, as set forth in that request, will place the issued patent in accordance with the record of the application as passed to issuance by the Examiner. Specifically, the requested corrections incorporate the cumulative amendments which were made to Table III of the specification in the Applicants' Amendment filed June 2, 2003, and Supplemental Amendment filed August 20, 2003, copies of which are submitted concurrently herewith.

Applicants respectfully request that the Certificate of Correction be issued in accordance with the corrections presented in the original request submitted on July 31, 2006.

Respectfully submitted,

Edward R. Ergenzinger
Registration No. 47,549

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Customer No. 00826	CERTIFICATE OF MAILING
ALSTON & BIRD LLP Bank of America Plaza 101 South Tryon Street, Suite 4000 Charlotte, NC 28280-4000 Tel Raleigh Office (919) 862-2200 Fax Charlotte Office (704) 444-1000	I hereby certify that this paper or fee is being deposited with the United States Postal Service First Class Mail service under 37 CFR 1.08 on the date indicated above and is addressed to Decisions & Certificate of Correction Branch, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 Karyn Grimm October 18, 2006 Date

LEGAL02/30101482v1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Hiatt, et al.

Title: NOVEL EPITHELIAL TISSUE
IMAGING AGENT

Appl. No.: 10/062,467

Filing Date: 02/05/2002

Examiner: David M. Naff

Art Unit: 1651

Mail Stop SEQUENCE
Commissioner for Patents
PO Box 1450
Alexandria, Virginia 22313-1450

AMENDMENT

Sir:

In response to the Office communication dated March 31, 2003 (Notice to Comply with Requirements for Patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence Disclosures), please consider the following amendments and remarks.

Amendments to the Specification begin on page 2 of this paper.

Remarks begin on page 11 of this paper.

023.236623.2

Application No.: 10/062,467
Filing Date: February 5, 2002
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Page 7 of 12

Attorney Docket No.: EPI3003C
(068904-0204)

SEQ ID NO:93 is synthetic peptide linker

Please replace Table III beginning on page 40, with the following replacement Table III.

-- TABLE III

Oligonucleotides for Construction of Representative Partial TM Genes

OLIGO	SEQUENCE
1:	gat cag gaa gat gaa cgt att gtt ctg gtt gac aac aag tgc aag tgt gct cgt att act t
2:	cta gaa gta ata cga gca cac ttg cac ttg ttg tca acc aga aca ata cgt tca tct tcc t
1.1:	gat cag aag tgc aag tgt gct cgt att act t
2.1:	ct aga agt aat acg agc aca ctt gca ctt ct
1.2ser:	gat cag gaa gat gaa cgt att gtt ctg gtt gac aac aag tgc aag tcc gct cgt att act t
2.2ser:	cta gaa gta ata cga gcg gac ttg cac ttg ttg tca acc aga aca ata cgt tca tct tcc t
1.2val:	gat cag gaa gat gaa cgt att gtt ctg gtt gac aac aag tgc aag gtt gct cgt att act t
2.2val:	cta gaa gta ata cga gca acc ttg cac ttg ttg tca acc aga aca ata cgt tca tct tcc t
3:	cta gaa tca tcc gta gct cag agg acc caa atg aag ata tag tcg aa
4	gat acg gat gtt acg ttc gac tat atc ttc att tgg gtc ctc tga gct acg gat gat t
5:	cgt aac atc cgt atc atc gtc cca ctg aat aac cgg gag aat atc tca g
5.1dg:	cgt aac atc cgt atc atc gtc cca ctg aat aac cgg gag cac atc tca g
6:	acg gac ttg tag gat ctg aga tat tct ccc ggt tat tca gtg gga cga t
6.1dg:	acg gac ttg tag gat ctg aga tgt gct ccc ggt tat tca gtg gga cga t
7:	atc cta caa gtc cgt tgc gca cac gct tcg tat acc acc tgt ca
8:	gat ctg aca ggt ggt ata cga agc gtg tgc gca
9:	gat ctg tgt aag aag tgt gat cca aca gag gta gag ctg gac aat cag ata gtc act gca
9L3Δ:	gat ctg tgt aag aag gat gag gac agc gct aca gaa acc tgc tg
10L3Δ:	aat tca gca ggt ttc tgt agc gct gtc ctc atc ctt ctt aca ca

Application No.: 10/062,467   Attorney Docket No.: EPI3003C
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In re application of Hiatt, et al.
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9L3ΔKDEL: gat ctg tgt aag aag gat gag gac agc gct aca gaa acc tgc tac gag aag
gat gag ctg tg

10L3ΔKDEL: aat tca cag ctc atc ctt cgc gtc gca ggt ttc tgt agc gct gtc ctc
atc ctt ctt aca ca

9.2Δ3:   gat ctg tgt aag aag tct gat atc gat gaa gat tcc gct aca gaa acc tgc
agc aca tg

10.2Δ3:   aat tca tgt gct gca ggt ttc tgt agc gga atc ttc atc gat atc aga ctt
ctt aca ca

9.3Δ3/ser68: gat ctg tct aag aag tct gat atc gat gaa gat tac aga ttc ttc aga
cta tag cta ctt cta a

10.3Δ3/ser68: aat ctt cat cga tat cag act tct tag aca

9.3Δ3/val68: gat ctg gtt aag aag tct gat atc gat gaa gat tac caa ttc ttc aga
cta tag cta ctt cta a

10.3Δ3/val68: aat ctt cat cga tat cag act tct taa cca

10:        att gtc cag ctc tac ctc tgt tgg atc aca ctt ctt aca ca

11:        act caa agc aac att tgc gat gag gac agc gct aca gaa acc tgc a

12:        ggt ttc tgt agc gct ctg ctc atc gca aat gtt gct ttg agt cgc agt gac
tat ctg

13:        gc acc tac gat agg aac aaa tgc tac acg gcc gtg gtt ccg ctc gtg tat
ggt gga gag

14:        gag cgg aac cac ggc cgt gta gca ttt gtt cct atc gta ggt gct gca

15:        aca aaa atg gtg gaa act gcc ctt acg ccc gat gca tgc tat .ccg gac tg

16:        aat tca gtc cgg ata gca tgc atc ggg cgt aag ggc agt ttc cac cat ttt
tgt ctc tcc acc ata cac

15KDEL: aca aaa atg gtg gaa act gcc ctt acg ccc gat gca tgc tat ccg gac aag
gat gaa ttg tg

16KDEL: aat tca caa ttc atc ctt gtc cgg ata gca tgc atc ggg cgt aag ggc agt
ttc cac cat ttt tgt ctc tcc acc ata cac

P1: gat cag gtc gct gcc atc caa gac ccg agg ctg ttc gcc gaa gag aag
gcc gtc gct gac tcc aag tgc aag tgt gct cgt att act t

P2:   ct aga agt aat acg agc aca ctt gca ctt gga gtc agc gac ggc ctt ctc

ttc ggc gaa cag cct cgg gtc ttg gat ggc agc gac ct

Tp1:   gc gat gac gac gat aag gcc caa acg gag acc tgt act gtt gcg cct cgt
gaa cgg caa aac tgc gga ttc ccg ~~gaa~~ gga

Application No.: 10/062,467   Attorney Docket No.: EPI3003C
Filing Date: February 5, 2002   (068904-0204)
In re application of Hiatt, et al.
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```
Tp2:    gtt ttg ccg ttc acg agg cgc aac agt aca ggt ctc cgt ttg ggc ctt atc
        gtc gtc atc gct tca gca                                                |

Tp3:    gta aca ccc tct cag tgc gct aat aaa ggc tgc tgt ttt gat gac acg gta
        cgg ggc gtt ccg tgg tgc tte ttt                                        |

Tp4:    gcc ccg tac cgt gtc atc aaa aca gca gcc ttt att agc gca ctg aga ggg
        tgt tac tte tcc cgg gaa tcc gca                                        |

Tp5:    tac ccc aat aca att gac gtt ccg cct gaa gaa gag tgc gag ccg taa g

Tp6:    aattc tta cgg ctc gca ctc ttc ttc agg cgg caa gtc aat tgt att ggg gta
        gaa aaa gca cca cgg aac                                                 |
```

Please replace Table X beginning on page 49, with the following replacement Table X.

-- Table X

DNA and Primary Amino Acid Sequence of TpS2

```
101 102
cys ser asp asp asp asp lys ala gln thr glu thr cys thr val ala pro
    gc gat gac gac gat aag gcc caa acg gag acc tgt act gtt gcg cct
act acg tcg cta ctg ctg cta ttc cgg gtt tgc ctc tgg aca tga caa cgc gga   |

arg glu arg gln asn cys gly phe pro gly val thr pro ser gln cys ala
cgt gaa cgg caa aac tgc gga ttc ccg gaa gga/gta aca ccc tct cag tgc gct   |
gca ctt gcc gtt ttg/acg cct aag ggc ett cct cat tgt ggg aga gtc acg cga   |

asn lys gly cys cys phe asp asp thr val arg gly val pro trp cys phe
aat aaa ggc tgc tgt ttt gat gac acg gta cgg ggc gtt ccg tgg tgc tte ttt/  |
tta ttt ccg acg aca aaa cta ctg tgc cat gcc ccg/caa ggc acc acg aag aaa   |

tyr pro asn thr ile asp val pro pro glu glu glu cys glu phe
tac ccc aat aca att gac gtt ccg cct gaa gaa gag tgc gag ccg taa g
atg ggg tta tgt taa ctg caa ggc gga ctt ctt ctc acg ctc ggc att cttaa --
```

Please replace paragraph [0119] with the following replacement paragraph [0119].

-- [0119] The important properties of the dyes are summarized in Tables X XI and XI XII. |

NOVEL EPITHELIAL TISSUE IMAGING AGENT

Cross-reference of Related Applications

[0001]   This application is a contination application of co-pending U.S. application Serial No. 09/005,167, filed 01/09/98, which is a continuation-in-part of U.S. application Serial No. 08/782,480, filed January 10, 1997, now U.S. Patent No. 6,045,774.

Technical Field

[0002]   The present invention relates generally to the targeting of diagnostic compounds to specific cells and tissues. The invention is more particularly related to targeting molecules for use in delivering compounds to epithelial tissue. Such targeting molecules may be used in a variety of diagnostic procedures.

Background of the Invention

[0003]   To improve the diagnosis of cancer and other disorders, some researchers have used the systemic administration of imaging agents (*e.g.*, proton relaxation agents as well as fluorescent chromophores) for contrast enhancement in techniques such as magnetic resonance imaging (MRI) and laser phototherapy. For example, tumor location using radiolabeled antibodies and handheld probes for intraoperative tumor detection has been attempted (Arnold et al., *Surgery 112*:624-631, 1992). Introduction of fluorescein conjugated antibodies for endoscopic tumor location ("photo-immunodiagnosis") in animals and in humans has also been attempted (Folli et al., *Cancer Res. 54*:2643-2450, 1994; Pelegrin et al., *Cancer 67*:2529-2535, 1994). In addition, fluorochrome-conjugated antibodies have been used to study antibody circulation in tumor microvasculature and biodistribution in tumors.

[0004]   While such techniques show promise, their use has been limited by a lack of agents or conjugates that show specific localization to particular cell types. For example, localization to cell populations that are frequent sites of neoplastic development would aid in the diagnosis of incipient tumors. Further selectivity for

TABLE III

Oligonucleotides for Construction of Representative Partial TM Genes

OLIGO	SEQUENCE
1:	gat cag gaa gat gaa cgt att gtt ctg gtt gac aac aag tgc aag tgt gct cgt att act t
2:	cta gaa gta ata cga gca cac ttg cac ttg ttg tca acc aga aca ata cgt tca tct tcc t
1.1:	gat cag aag tgc aag tgt gct cgt att act t
2.1:	ct aga agt aat acg agc aca ctt gca ctt ct
1.2ser:	gat cag gaa gat gaa cgt att gtt ctg gtt gac aac aag tgc aag tcc gct cgt att act t
2.2ser:	cta gaa gta ata cga gcg gac ttg cac ttg ttg tca acc aga aca ata cgt tca tct tcc t
1.2val:	gat cag gaa gat gaa cgt att gtt ctg gtt gac aac aag tgc aag gtt gct cgt att act t
2.2val:	cta gaa gta ata cga gca acc ttg cac ttg ttg tca acc aga aca ata cgt tca tct tcc t
3:	cta gaa tca tcc gta gct cag agg acc caa atg aag ata tag tcg aa
4	gat acg gat gtt acg ttc gac tat atc ttc att tgg gtc ctc tga gct acg gat gat t
5:	cgt aac atc cgt atc atc gtc cca ctg aat aac cgg gag aat atc tca g

5.1dg: cgt aac atc cgt atc atc gtc cca ctg aat aac cgg gag cac atc

tca g

6:        acg gac ttg tag gat ctg aga tat tct ccc ggt tat tca gtg gga

cga t

6.1dg: acg gac ttg tag gat ctg aga tgt gct ccc ggt tat tca gtg gga

cga t

7:        atc cta caa gtc cgt tgc gca cac gct tcg tat acc acc tgt ca

8:        gat ctg aca ggt ggt ata cga agc gtg tgc gca

9:        gat ctg tgt aag aag tgt gat cca aca gag gta gag ctg gac aat

cag ata gtc act gca

9L3Δ: gat ctg tgt aag aag gat gag gac agc gct aca gaa acc tgc tg

10L3Δ: aat tca gca ggt ttc tgt agc gct gtc ctc atc ctt ctt aca ca

9L3ΔKDEL: gat ctg tgt aag aag gat gag gac agc gct aca gaa acc tgc tac

gag aag gat gag ctg tg

10L3ΔKDEL: aat tca cag ctc atc ctt cgc gtc gca ggt ttc tgt agc gct gtc

ctc atc ctt ctt aca ca

9.2Δ3:   gat ctg tgt aag aag tct gat atc gat gaa gat tcc gct aca gaa

acc tgc agc aca tg

10.2Δ3:   aat tca tgt gct gca ggt ttc tgt agc gga atc ttc atc gat atc

aga ctt ctt aca ca

9.3Δ3/ser68:   gat ctg tct aag aag tct gat atc gat gaa gat tac aga ttc ttc

aga cta tag cta ctt cta a

10.3Δ3/ser68:   aat ctt cat cga tat cag act tct tag aca

9.3Δ3/val68:   gat ctg gtt aag aag tct gat atc gat gaa gat tac caa ttc ttc

aga cta tag cta ctt cta a

10.3Δ3/val68:   aat ctt cat cga tat cag act tct taa cca

10:             att gtc cag ctc tac ctc tgt tgg atc aca ctt ctt aca ca

11:             act caa agc aac att tgc gat gag gac agc gct aca gaa acc tgc a

12:             ggt ttc tgt agc gct ctg ctc atc gca aat gtt gct ttg agt cgc

agt gac tat ctg

13:             gc acc tac gat agg aac aaa tgc tac acg gcc gtg gtt ccg ctc

gtg tat ggt gga gag

14:             gag cgg aac cac ggc cgt gta gca ttt gtt cct atc gta ggt gct

gca

15:             aca aaa atg gtg gaa act gcc ctt acg ccc gat gca tgc tat ccg

gac tg

16:             aat tca gtc cgg ata gca tgc atc ggg cgt aag ggc agt ttc cac

cat ttt tgt ctc tcc acc ata cac

15KDEL: aca aaa atg gtg gaa act gcc ctt acg ccc gat gca tgc tat ccg

gac aag gat gaa ttg tg

16KDEL: aat tca caa ttc atc ctt gtc cgg ata gca tgc atc ggg cgt aag

ggc agt ttc cac cat ttt tgt ctc tcc acc ata cac

P1:   gat cag gtc gct gcc atc caa gac ccg agg ctg ttc gcc gaa gag

aag gcc gtc gct gac tcc aag tgc aag tgt gct cgt att act t

P2:   ct aga agt aat acg agc aca ctt gca ctt gga gtc agc gac ggc

ctt ctc ttc ggc gaa cag cct cgg gtc ttg atg ggc agc gac ct

Tp1:   gc gat gac gac gat aag gcc caa acg gag acc tgt act gtt gcg cct cgt gaa
         cgg caa aac tgc gga ttc ccg gaa

Tp2:   gtt ttg ccg ttc acg agg cgc aac agt aca ggt ctc cgt ttg ggc ctt atc
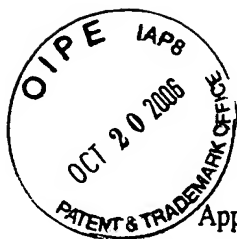   gtc gtc atc gct tca

Tp3:   gta aca ccc tct cag tgc gct aat aaa ggc tgc tgt ttt gat gac acg gta
         cgg ggc gtt ccg tgg tgc ttc

Tp4:   gcc ccg tac cgt gtc atc aaa aca gca gcc ttt att agc gca ctg aga ggg
         tgt tac ttc cgg gaa tcc gca

Tp5:   tac ccc aat aca att gac gtt ccg cct gaa gaa gag tgc gag ccg taa g

Tp6:   aattc tta cgg ctc gca ctc ttc ttc agg cgg caa gtc aat tgt att ggg
         gta gaa gca cca cgg aac

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
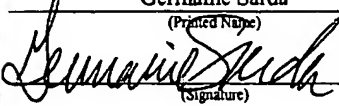
Applicant: Hiatt, et al.

Title: NOVEL EPITHELIAL TISSUE
        IMAGING AGENT

Appl. No.:   10/062,467

Filing Date: 02/05/2002

Examiner: David M. Naff

Art Unit: 1651

SUPPLEMENTAL AMENDMENT

Mail Stop SEQUENCE
Commissioner for Patents
PO Box 1450
Alexandria, Virginia 22313-1450

Sir:

Please amend the application as indicated below.

Amendments to the Specification begin on page 2 of this paper.

Remarks begin on page 5 of this paper.

DLMR236623.2

Amendments to the Specification

Please replace the previous Sequence Listing with the new Sequence Listing submitted herewith.

Please replace Table III beginning on page 40, with the following replacement Table III. Please note that the changes to Table III are shown relative to the Table III as filed.

TABLE III

Oligonucleotides for Construction of Representative Partial TM Genes

OLIGO	SEQUENCE
1:	gat cag gaa gat gaa cgt att gtt ctg gtt gac aac aag tgc aag tgt gct cgt att act t
2:	cta gaa gta ata cga gca cac ttg cac ttg ttg tca acc aga aca ata cgt tca tct tcc t
1.1:	gat cag aag tgc aag tgt gct cgt att act t
2.1:	ct aga agt aat acg agc aca ctt gca ctt ct
1.2ser:	gat cag gaa gat gaa cgt att gtt ctg gtt gac aac aag tgc aag tcc gct cgt att act t
2.2ser:	cta gaa gta ata cga gcg gac ttg cac ttg ttg tca acc aga aca ata cgt tca tct tcc t
1.2val:	gat cag gaa gat gaa cgt att gtt ctg gtt gac aac aag tgc aag gtt gct cgt att act t
2.2val:	cta gaa gta ata cga gca acc ttg cac ttg ttg tca acc aga aca ata cgt tca tct tcc t
3:	cta gaa tca tcc gta gct cag agg acc caa atg aag ata tag tcg aa
4	gat acg gat gtt acg ttc gac tat atc ttc att tgg gtc ctc tga gct acg gat gat t
5:	cgt aac atc cgt atc atc gtc cca ctg aat aac cgg gag aat atc tca g
5.1dg:	cgt aac atc cgt atc atc gtc cca ctg aat aac cgg gag cac atc tca g
6:	acg gac ttg tag gat ctg aga tat tct ccc ggt tat tca gtg gga cga t
6.1dg:	acg gac ttg tag gat ctg aga tgt gct ccc ggt tat tca gtg gga cga t
7:	atc cta caa gtc cgt tgc gca cac gct tcg tat acc acc tgt ca
8:	gat ctg aca ggt ggt ata cga agc gtg tgc gca

Application No.: 10/062,467   Attorney Docket No.: EPI3003C
Filing Date: February 5, 2002   (068904-0204)
In re application of Hiatt, et al.
Page 3 of 6

9:       gat ctg tgt aag aag tgt gat cca aca gag gta gag ctg gac aat cag ata
gtc act gca

9L3Δ: gat ctg tgt aag aag gat gag gac agc gct aca gaa acc tgc tg

10L3Δ: aat tca gca ggt ttc tgt agc gct gtc ctc atc ctt ctt aca ca

9L3ΔKDEL: gat ctg tgt aag aag gat gag gac agc gct aca gaa acc tgc tac gag aag
gat gag ctg tg

10L3ΔKDEL: aat tca cag ctc atc ctt cgc gtc gca ggt ttc tgt agc gct gtc ctc
atc ctt ctt aca ca

9.2Δ3:   gat ctg tgt aag aag tct gat atc gat gaa gat tcc gct aca gaa acc tgc
agc aca tg

10.2Δ3:   aat tca tgt gct gca ggt ttc tgt agc gga atc ttc atc gat atc aga ctt
ctt aca ca

9.3Δ3/ser68: gat ctg tct aag aag tct gat atc gat gaa gat tac aga ttc ttc aga
cta tag cta ctt cta a

10.3Δ3/ser68: aat ctt cat cga tat cag act tct tag aca

9.3Δ3/val68: gat ctg gtt aag aag tct gat atc gat gaa gat tac caa ttc ttc aga
cta tag cta ctt cta a

10.3Δ3/val68: aat ctt cat cga tat cag act tct taa cca

10:       att gtc cag ctc tac ctc tgt tgg atc aca ctt ctt aca ca

11:       act caa agc aac att tgc gat gag gac agc gct aca gaa acc tgc a

12:       ggt ttc tgt agc gct ctg ctc atc gca aat gtt gct ttg agt cgc agt gac
tat ctg

13:       gc acc tac gat agg aac aaa tgc tac acg gcc gtg gtt ccg ctc gtg tat
ggt gga gag

14:       gag cgg aac cac ggc cgt gta gca ttt gtt cct atc gta ggt gct gca

15:       aca aaa atg gtg gaa act gcc ctt acg ccc gat gca tgc tat ccg gac tg

16:       aat tca gtc cgg ata gca tgc atc ggg cgt aag ggc agt ttc cac cat ttt
tgt ctc tcc acc ata cac

15KDEL: aca aaa atg gtg gaa act gcc ctt acg ccc gat gca tgc tat ccg gac aag
gat gaa ttg tg

16KDEL: aat tca caa ttc atc ctt gtc cgg ata gca tgc atc ggg cgt aag ggc agt
ttc cac cat ttt tgt ctc tcc acc ata cac

              P1: gat cag gtc gct gcc atc caa gac ccg agg ctg ttc gcc gaa gag aag
gcc gtc gct gac tcc aag tgc aag tgt gct cgt att act t

P2:   ct aga agt aat acg agc aca ctt gca ctt gga gtc agc gac ggc ctt ctc

```
        ttc ggc gaa cag cct cgg gtc ttg gat ggc agc gac ct

Tp1:    gc gat gac gac gat aag gcc caa acg gag acc tgt act gtt gcg cct cgt
        gaa cgg caa aac tgc gga ttc ccg gaa gga

Tp2:    gtt ttg ccg ttc acg agg cgc aac agt aca ggt ctc cgt ttg ggc ctt atc
        gtc gtc atc gct tca gca

Tp3:    gta aca ccc tct cag tgc gct aat aaa ggc tgc tgt ttt gat gac acg gta
        cgg ggc gtt ccg tgg tgc ttc

Tp4:    gcc ccg tac cgt gtc atc aaa aca gca gcc ttt att agc gca ctg aga ggg
        tgt tac tto tcc cgg gaa tcc gca

Tp5:    tac ccc aat aca att gac gtt ccg cct gaa gaa gag tgc gag ccg ttt taa g

Tp6:    aattc tta cgg ctc gca ctc ttc ttc agg cgg caa gtc aat tgt att ggg gta
        gaa gca cca cgg aaa aac
```

Please replace Table X beginning on page 49, with the following replacement Table X.

Please note that the changes to Table III are shown relative to the Table III as filed.

<u>Table X</u>

<u>DNA and Primary Amino Acid Sequence of TpS2</u>

```
101 102
cys ser asp asp asp asp lys ala gln thr glu thr cys thr val ala pro
    gc gat gac gac gat aag gcc caa acg gag acc tgt act gtt gcg cct
act acg tcg cta ctg ctg cta ttc cgg gtt tgc ctc tgg aca tga caa cgc gga

arg glu arg gln asn cys gly phe pro gly val thr pro ser gln cys ala
cgt gaa cgg caa aac tgc gga ttc ccg gaa gga/gta aca ccc tct cag tgc gct
gca ctt gcc gtt ttg/acg cct aag ggc ctt cct cat tgt ggg aga gtc acg cga

asn lys gly cys cys phe asp asp thr val arg gly val pro trp cys phe
aat aaa ggc tgc tgt ttt gat gac acg gta cgg ggc gtt ccg tgg tgc ttc/
tta ttt ccg acg aca aaa cta ctg tgc cat gcc ccg/caa ggc acc acg aag

tyr pro asn thr ile asp val pro pro glu glu glu cys glu phe
tac ccc aat aca att gac gtt ccg cct gaa gaa gag tgc gag ccg ttt taa g
atg ggg tta tgt taa ctg caa ggc gga ctt ctt ctc acg ctc gge aaa att
cttaa --
```

Remarks

A new Sequence Listing paper copy and computer disk are filed herewith to correct informalities in the previously filed Sequence Listing. The specification has been amended herein to correct typographical errors in certain DNA sequences. The new version of Table III amends Tp1 (SEQ ID NO: 87), Tp2 (SEQ ID NO: 88), Tp4 (SEQ ID NO: 90), Tp5 (SEQ ID NO: 91), and Tp6 (SEQ ID NO: 92). Also amended is Table X - Tp2 DNA sequence (SEQ ID NOs. 16 and 36). Basis for the changes is as follows. Please note that all references to nucleotide bases are from 5' to 3'.

In the last base in the first codon of the anti-sense strand of the double stranded DNA sequence shown in Table X was modified from a "t" to "g." This changes the codon from act, the anti-sense of a stop codon, to acg, the anti-sense of the codon tgc which encodes cytseine, the amino acid indicated to be encoded in table X. No new matter is implicated by this change as the anti-sense codon has been conformed to be complementary to the proper codon of the sense strand to encode the amino acid sequence indicated in the table. This change to the anti-sense strand codon relating to the specified cys residue of Table X has also been made to the corresponding codon in the Tp2 sequence seen in Table III (i.e., tca to gca).

The middle base in what is the sense strand for codon 127 encoding gly (within the sequence pro-gly-val) of the double stranded DNA sequence of Table X has been changed from "a" to "g." Thus, the codon gaa has been changed to gga to properly encode the indicated amino acid glycine. Support for the gly residue at position 127 in Table X is found in the specification at page 37, paragraph [0115] (citing to Suemeri et al., PNAS 88:11017-11021, 1991 for the sequence of TpS2) and by Suemeri et al., Fig. 3 (copy previously attached), which shows a gly in the same position for TpS2. No new matter is implicated by this change as the encoding DNA sequence has been conformed to the amino acid sequence of the table. The anti-sense strand codon that corresponds to this change also has been changed from ctt to cct. No new matter is added as this change is predicted by Watson-Crick base pairing to the sequence of the sense strand. These changes to the sense and anti-sense strand codons relating to the specified gly

residue of Table X have also been made to the corresponding codons in the Tp1 and Tp4
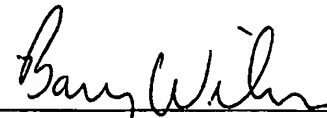
sequences, respectively, as seen in Table III.

The codon for the C- terminal most phe of the double stranded DNA sequence of Table X

has been changed from "ccg" (pro) to "ttt" (phe). Thus, the codon ccg has been changed to ttt to

properly encode the indicated amino acid phenylalanine (phe). Support for the C-terminal most

phe in Table X is found in the specification at page 37, paragraph [0115] (citing to Suemeri et

al., PNAS 88:11017-11021, 1991 for the sequence of TpS2) and by Suemeri et al., Fig. 3 (copy

previously attached), which shows a phe at the end of the sequence for TpS2. No new matter is

implicated by this change as the encoding DNA sequence has been conformed to the amino acid

sequence of the table. The anti-sense strand codon that corresponds to this change also has been

changed from cgg to aaa. No new matter is added as this change is predicted by Watson-Crick

base pairing to the sequence of the sense strand. These changes to the sense and anti-sense

strand codons relating to the specified phe residue of Table X have also been made to the

corresponding codons in the Tp3 and Tp6 sequences, respectively, as seen in Table III.

The new Sequence Listing paper copy and computer disk reflect the sequence changes

discussed above. Thus, the amendments to the specification raise no issue of new matter.

Respectfully submitted,

By

Date _____August 20, 2003_____

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